Amendments to the Claims:

This listing of claims will replace all prior versions and listings of claims in the application. Please cancel claims 1-79. Please add new claim 80-88.

Listing of Claims:

1. - 79. (Canceled)

80. (New) A ligand-activated uni-molecular detector comprising:

a circularly permutated marker protein comprising a first interactor domain covalently bonded to the circularly permutated marker protein through an N-terminal breakpoint of the circularly permutated marker protein and a second interactor domain covalently bonded to the circularly permutated marker protein through a C-terminal breakpoint circularly permutated of the marker protein, wherein said circularly permutated marker protein is functionally reconstituted only upon binding of said first interactor domain and said second interactor domain to a single ligand.

81. (New) The ligand-activated uni-molecular detector of claim 80, wherein said circularly permutated marker protein is a circularly permutated enzyme.

82. (New) The ligand-activated uni-molecular detector of claim 81, wherein said circularly permutated enzyme is a β-lactamase protein.

83. (New) The ligand-activated uni-molecular detector of claim 82, wherein said circularly permutated enzyme is a TEM-1 β-lactamase protein.

84. (New) The ligand-activated uni-molecular detector of claim 80, wherein said N-terminal break point and said C-terminal break point are within a solvent exposed loop between elements of secondary structure within the enzyme.

85. (New) The ligand-activated uni-molecular detector of claim 80, wherein said circularly permutated protein is a β-lactamase protein comprising amino acids 1 to 263 of SEQ

ID: NO 2, wherein said N-terminal breakpoint and said C-terminal breakpoint are within 10 amino acids of an amide bond junction between two amino acids selected from the group consisting of asparagine 52 and serine 53, leucine 91 and glycine 92, glutamine 99 and asparagine 100, proline 174 and asparagine 175, glutamic acid 197 and leucine 198, lysine 215 and valine 216, alanine 227 and glycine 228, and glycine 253 and lysine 254.

86. (New) The ligand-activated uni-molecular detector of claim 85, wherein said two amino acids are selected from the group consisting of proline 174 and asparagine 175, glutamic acid 197 and leucine 198, lysine 215 and valine 216, alanine 227 and glycine 228, and glycine 253 and lysine 254.

87. (New) The ligand-activated uni-molecular detector of claim 85, wherein said two amino acids are glutamic acid 197 and leucine 198.

88. (New) The ligand-activated uni-molecular detector of claim 80, wherein said ligand is a protein ligand.

89. (New) A method of detecting the presence of a target ligand using a ligand-activated uni-molecular detector comprising the steps of:

(a) contacting said target ligand with said ligand-activated uni-molecular detector, said ligand-activated uni-molecular detector comprising a circularly permutated marker protein comprising a first interactor domain covalently bonded to the circularly permutated marker protein through an N-terminal breakpoint of the circularly permutated marker protein and a second interactor domain covalently bonded to the circularly permutated marker protein through a C-terminal breakpoint of the circularly permutated marker protein;

(b) allowing said target ligand to bind to said first interactor domain and said second interactor domain;

(c) after step (b), allowing said circularly permutated marker protein to functionally reconstitute;

(d) detecting the functionally reconstituted circularly permutated marker protein thereby detecting the presence of said target ligand.